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IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

Applicant : Fang. et al.
Art Unit : 1648
Serial No. : 09/910,483
Examiner : NYA
Filed : July 19, 2001
Title : HUMANIZED ANTIBODIES

Commissioner for Patents
Washington, D.C. 20231

PRELIMINARY AMENDMENT

Sir:

Prior to examination of the above-identified application, please amend the specification as follows:

IN THE SPECIFICATION

At page 1, line 6, please delete May 31, 2001 and insert therefore —August 16, 2000—.

REMARKS

The amendment to the specification was made to provide the correct priority application filing date, in accordance with 37 CFR §1.78. The amendment therefore was made to address an informality and, as such does not add new matter. Entry of the amendment is respectfully requested. A clean copy of page 1 is furnished herewith. The clean copy includes the correct priority application filing date.

Respectfully submitted,

Date: 9-17-01

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Humanized Antibodies

RELATED APPLICATIONS

This application is a continuation-in-part and claims the benefit of priority of application serial no. 09/555,446, filed August 16, 2000, which is a 35 U.S.C. 371 of PCT application serial no. PCT/US98/25422, filed November 30, 1998.

FIELD OF THE INVENTION

The invention relates to humanized antibody compositions and methods of making and using humanized antibodies.

BACKGROUND

Monoclonal antibodies have become an important class of therapeutic proteins. However, foreign immunoglobulins used in humans can elicit an anti-globulin response which may interfere with therapy or cause allergic or immune complex hypersensitivity. To avoid this problem, a monoclonal antibody may be "humanized," and this is typically carried out by CDR grafting.

CDR's, also called hypervariable regions, are present in immunoglobulin light and heavy chains and are flanked by "framework" regions. CDR grafting was first described in Jones *et al.* ((1986) *Nature* 321:522-525). In this and later publications, the CDRs of three mouse antibodies were grafted onto the variable domain frameworks of the human immunoglobulin NEW (V_H) and REI (V_L). The resulting humanized antibodies had the same antigen specificity and a similar affinity as the parental murine monoclonal antibody (mAb) (Jones *et al. supra*; Verhoeyen *et al.* (1988) *Science* 239:1534-1536; Riechmann *et al.* (1988) *Nature* 332:323-327; U.S. Patent No. 5,225,539).

CDR grafting has been described by Queen and coworkers who reported the humanization of four murine monoclonal antibodies (Queen *et al.* (1989) *Proc. Natl. Acad. Sci. USA* 86:10029-10033; Co *et al.* (1991) *Proc. Natl. Acad. Sci. USA* 88:2869-2873; Co *et al.* (1992) *J. Immunol.*148:1149-1154; and U.S. Patent Nos. 5,585,089; 5,693,761; and 5,693,762). Murine residues were inserted in the human framework in order to maintain affinity and, in each case the original antigen specificity was